

CLAIMS

1. A method for treating a subject for skin disorder comprising administering to
5 said subject an effective amount of creatine, creatine phosphate, creatine compound or a salt thereof, such that said skin disorder is treated.

2. The method of claim 1, wherein said subject is a mammal.

10 3. The method of claim 1, wherein said subject is a human.

4. The method of claim 1, further comprising coadministration of a
pharmaceutically acceptable carrier.

15 5. The method of claim 4, wherein said pharmaceutically acceptable carrier is suitable for topical administration.

6. The method of claim 1 wherein said skin disorder is associated with free-
radicals.

20 7. The method of claim 1, wherein said skin disorder is associated with aging.

8. The method of claim 1 wherein said skin disorder is associated with sun
radiation.

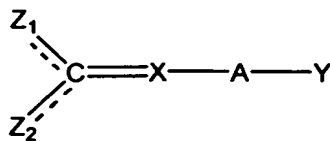
25 9. The method of claim 1 wherein said skin disorder is associated with stress or fatigue.

10. The method of claim 1, wherein said subject is afflicted with skin wrinkles.

30 11. The method of claim 1, wherein said subject is at risk for a skin disorder.

12. A method for treatment of a skin disorder comprising administering an
effective amount of a creatine compound to a subject such that the subject is treated, wherein
35 the creatine compound is of the general formula:

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and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{NO}_2$, $-\text{SO}_3\text{H}$, $-\text{C}(=\text{O})\text{NHSO}_2\text{J}$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, C_1 - C_6 straight chain alkyl, C_3 - C_6 branched alkyl, C_2 - C_6 alkenyl, C_3 - C_6 branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C_1 - C_5 alkyl, C_2 - C_5 alkenyl, C_2 - C_5 alkynyl, and C_1 - C_5 alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group selected from the group consisting of: a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) $-\text{NH}-\text{M}$, wherein M is selected from the group consisting of: hydrogen, C_1 - C_4 alkyl, C_2 - C_4 alkenyl, C_1 - C_4 alkoyl, C_3 - C_4 branched alkyl, C_3 - C_4 branched alkenyl, and C_4 branched alkoyl;

c) X is selected from the group consisting of NR_1 , CHR_1 , CR_1 , O and S, wherein R_1 is selected from the group consisting of:

1) hydrogen;

2) K where K is selected from the group consisting of: C_1 - C_6 straight alkyl, C_2 - C_6 straight alkenyl, C_1 - C_6 straight alkoyl, C_3 - C_6 branched alkyl, C_3 - C_6 branched alkenyl, and C_4 - C_6 branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a $\text{C}_5\text{-C}_9$ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

5) a $\text{C}_5\text{-C}_9$ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

6) a $\text{C}_5\text{-C}_9$ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z_1 and Z_2 are chosen independently from the group consisting of: $=\text{O}$, $-\text{NHR}_2$, $-\text{CH}_2\text{R}_2$, $-\text{NR}_2\text{OH}$; wherein Z_1 and Z_2 may not both be $=\text{O}$ and wherein R_2 is selected from the group consisting of:

1) hydrogen;

2) K, where K is selected from the group consisting of: $\text{C}_1\text{-C}_6$ straight alkyl; $\text{C}_2\text{-C}_6$ straight alkenyl, $\text{C}_1\text{-C}_6$ straight alkoyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_3\text{-C}_6$ branched alkenyl, and $\text{C}_4\text{-C}_6$ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: $-\text{CH}_2\text{L}$ and $-\text{COCH}_2\text{L}$ where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a $\text{C}_4\text{-C}_8$ a-amino-carboxylic acid attached via the w-carbon;

5) B, wherein B is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{SO}_3\text{H}$, $-\text{NO}_2$, $\text{OP}(=\text{O})(\text{OH})(\text{OJ})$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, $\text{C}_1\text{-C}_6$ straight alkyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_3\text{-C}_6$ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: $\text{C}_1\text{-C}_2$ alkyl, C_2 alkenyl, and $\text{C}_1\text{-C}_2$ alkoyl;

6) -D-E, wherein D is selected from the group consisting of: C₁-C₃ straight alkyl, C₃ branched alkyl, C₂-C₃ straight alkenyl, C₃ branched alkenyl, C₁-C₃ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: -(PO₃)_nNMP, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) -E, wherein E is selected from the group consisting of - (PO₃)_nNMP, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; -[P(=O)(OCH₃)(O)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; -[P(=O)(OH)(CH₂)]_m-Q, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, -OG, -C(=O)G, and -CO₂G, where G is independently selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, C₄-C₆ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R₁ and at least one R₂ group are present, R₁ may be connected by a single or double bond to an R₂ group to form a cycle of 5 to 7 members;

f) if two R₂ groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R₁ is present and Z₁ or Z₂ is selected from the group consisting of -NHR₂, -CH₂R₂ and -NR₂OH, then R₁ may be connected by a single or double bond to the carbon or nitrogen of either Z₁ or Z₂ to form a cycle of 4 to 7 members.

13. The method of claim 12, wherein said treatment of said skin disorder reduces or eliminates at least one preexisting symptom of skin disorder.

14. The method of claim 13, wherein said symptom is skin wrinkles or a loss of skin elasticity.

5 15. The method of claim 12, wherein said treatment of said skin disorder comprises prevention said skin disorder.

16. The method of claim 12, wherein said creatine compound is creatine.

10 17. The method of claim 12, wherein said creatine compound is creatine phosphate.

18. The method of claim 12, wherein said creatine compound is cyclocreatine.

15 19. The method of claim 12, wherein said creatine compound is cyclocreatine phosphate.

20 20. The method of claim 12, wherein said creatine compound is creatine-pyruvate.

20 21. The method of claim 12, wherein said creatine compound is creatine-ascorbate.

22. The method of claim 12, wherein said creatine compound is homocyclocreatine.

25 23. The method of claim 12, wherein said creatine compound is 3-guanidinopropionic acid.

24. The method of claim 12, wherein said creatine compound is guanidinoacetate.

30 25. The method of claim 12, wherein said creatine compound is a guanidino benzoic acid.

35 26. The method of claim 12, further comprising co-administering to said subject an effective amount of a skin preserving agent.

27. The method of claim 26, wherein said skin preserving agent is an antioxidant.

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28. The method of claim 27, wherein said antioxidant is CoQ10 or vitamin E.

29. The method of claim 26, wherein the skin preserving agent is an energy-enhancing agent.

30. The method of claim 29, wherein said energy enhancing agent is selected from the group consisting of ATP, nicotinamide and pyruvate.

31. The method of claim 26, wherein said skin preserving agent is a vitamin or a vitamin precursor.

32. The method of claim 31, wherein said vitamin is selected from the group consisting of E, C, B5, B6, and B9.

33. The method of claim 12, further comprising the coadministration of a pharmaceutical carrier suitable for topical administration.

34. The method of claim 33, wherein said creatine compound is administered in a lotion, cream, or ointment, gel or solid.

35. The method of claim 12, further comprising the coadministration of a sunscreen or sunblock.

36. The method of claim 35, wherein said sunscreen or sunblock is zinc oxide or titanium dioxide.

37. A composition for the treatment of the skin of a subject, comprising an effective amount of creatine, creatine phosphate, a creatine compound or a salt thereof, and a pharmaceutically acceptable carrier.

38. The composition of claim 37, wherein said composition is suitable for topical administration.

39. The composition of claim 38, wherein said composition is a lotion, cream, or ointment, gel or solid.

40. The composition of claim 37, wherein said composition further comprises a sunblock or sunscreen.

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42. The composition of claim 37, wherein said composition is formulated as a cosmetic foundation.

43. The composition of claim 37, further comprising a penetration agent.

44. The composition of claim 37, wherein said composition is formulated as a skin cleansing agent.

45. The composition of claim 37, wherein said composition further comprises hydroxyacids, retinols, Aloe, Chamomile, or mixtures thereof.

46. The composition of claim 37, wherein said effective amount is effective to treat skin disorder.

47. The composition of claim 46, wherein said skin disorder is associated with free-radicals.

48. The composition of claim 37, wherein said skin disorder is associated with aging, sun radiation, stress or fatigue.

49. The composition of claim 37, wherein said effective amount is effective to prevent a skin disorder.

50. The composition of claim 37, wherein said creatine compound is creatine.

51. The composition of claim 37, wherein said creatine compound is creatine phosphate.

52. The composition of claim 37, wherein said creatine compound is cyclocreatine.

53. The composition of claim 37, wherein said creatine compound is cyclocreatine phosphate.

54. The composition of claim 37, wherein said creatine compound is creatine-pyruvate.

55. The composition of claim 37, wherein said creatine compound is creatine-ascorbate.

56. The composition of claim 37, wherein said creatine compound is homocyclocreatine.

57. The composition of claim 37, wherein said creatine compound is 3-guanidinopropionic acid.

58. The composition of claim 37, wherein said creatine compound is guanidinoacetate.

59. The composition of claim 37, wherein said creatine compound is a guanidino benzoic acid.

60. The composition of claim 37, further comprising co-administering to said subject an effective amount of a skin preserving agent.

61. The composition of claim 60, wherein said skin preserving agent is an antioxidant.

62. The composition of claim 61, wherein said antioxidant is CoQ10 or vitamin E.

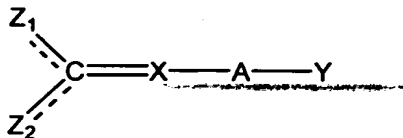
63. The composition of claim 60, wherein the skin preserving agent is an energy-enhancing agent.

64. The method of claim 63, wherein said energy enhancing agent is selected from the group consisting of ATP, nicotinamide and pyruvate.

65. The method of claim 64, wherein said skin preserving agent is a vitamin or a vitamin precursor.

66. The method of claim 65, wherein said vitamin is selected from the group consisting of E, C, B5, B6, and B9.

67. A composition for treatment of a skin disorder comprising an effective amount of a creatine compound and a pharmaceutical carrier suitable for topical administration, wherein said creatine compound is of the general formula:



5 and pharmaceutically acceptable salts thereof, wherein:

a) Y is selected from the group consisting of: -CO₂H, -NHOH, -NO₂, -SO₃H, -C(=O)NHSO₂J and -P(=O)(OH)(OJ), wherein J is selected from the group consisting of: hydrogen, C₁-C₆ straight chain alkyl, C₃-C₆ branched alkyl, C₂-C₆ alkenyl, C₃-C₆ branched alkenyl, and aryl;

b) A is selected from the group consisting of: C, CH, C₁-C₅alkyl, C₂-C₅alkenyl, C₂-C₅alkynyl, and C₁-C₅ alkoyl chain, each having 0-2 substituents which are selected independently from the group consisting of:

1) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

2) an aryl group selected from the group consisting of: a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy; and

3) -NH-M, wherein M is selected from the group consisting of: hydrogen, C₁-C₄ alkyl, C₂-C₄ alkenyl, C₁-C₄ alkoyl, C₃-C₄ branched alkyl, C₃-C₄ branched alkenyl, and C₄ branched alkoyl;

c) X is selected from the group consisting of NR₁, CHR₁, CR₁, O and S, wherein R₁ is selected from the group consisting of:

1) hydrogen;

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2) K where K is selected from the group consisting of: C₁-C₆ straight alkyl, C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₅-C₉ a-amino-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

5) a C₅-C₉ a-amino-w-aza-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon; and

6) a C₅-C₉ a-amino-w-thia-w-methyl-w-adenosylcarboxylic acid attached via the w-methyl carbon;

d) Z₁ and Z₂ are chosen independently from the group consisting of: =O, -NHR₂, -CH₂R₂, -NR₂OH; wherein Z₁ and Z₂ may not both be =O and wherein R₂ is selected from the group consisting of:

1) hydrogen;

2) K, where K is selected from the group consisting of: C₁-C₆ straight alkyl; C₂-C₆ straight alkenyl, C₁-C₆ straight alkoyl, C₃-C₆ branched alkyl, C₃-C₆ branched alkenyl, and C₄-C₆ branched alkoyl, K having 0-2 substituents independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

3) an aryl group selected from the group consisting of a 1-2 ring carbocycle and a 1-2 ring heterocycle, wherein the aryl group contains 0-2 substituents independently selected from the group consisting of: -CH₂L and -COCH₂L where L is independently selected from the group consisting of: bromo, chloro, epoxy and acetoxy;

4) a C₄-C₈ a-amino-carboxylic acid attached via the w-carbon;

5) B, wherein B is selected from the group consisting of: $-\text{CO}_2\text{H}$, $-\text{NHOH}$, $-\text{SO}_3\text{H}$, $-\text{NO}_2$, $\text{OP}(=\text{O})(\text{OH})(\text{OJ})$ and $-\text{P}(=\text{O})(\text{OH})(\text{OJ})$, wherein J is selected from the group consisting of: hydrogen, $\text{C}_1\text{-C}_6$ straight alkyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_2\text{-C}_6$ alkenyl, $\text{C}_3\text{-C}_6$ branched alkenyl, and aryl, wherein B is optionally connected to the nitrogen via a linker selected from the group consisting of: $\text{C}_1\text{-C}_2$ alkyl, C_2 alkenyl, and $\text{C}_1\text{-C}_2$ alkoyl;

6) -D-E, wherein D is selected from the group consisting of: $\text{C}_1\text{-C}_3$ straight alkyl, C_3 branched alkyl, $\text{C}_2\text{-C}_3$ straight alkenyl, C_3 branched alkenyl, $\text{C}_1\text{-C}_3$ straight alkoyl, aryl and aroyl; and E is selected from the group consisting of: $-(\text{PO}_3)_n\text{NMP}$, where n is 0-2 and NMP is ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OCH}_3)(\text{O})]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OH})(\text{CH}_2)]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, $-\text{OG}$, $-\text{C}(=\text{O})\text{G}$, and $-\text{CO}_2\text{G}$, where G is independently selected from the group consisting of: $\text{C}_1\text{-C}_6$ straight alkyl, $\text{C}_2\text{-C}_6$ straight alkenyl, $\text{C}_1\text{-C}_6$ straight alkoyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_3\text{-C}_6$ branched alkenyl, $\text{C}_4\text{-C}_6$ branched alkoyl, wherein E may be attached to any point to D, and if D is alkyl or alkenyl, D may be connected at either or both ends by an amide linkage; and

7) -E, wherein E is selected from the group consisting of: $(\text{PO}_3)_n\text{NMP}$, where n is 0-2 and NMP is a ribonucleotide monophosphate connected via the 5'-phosphate, 3'-phosphate or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OCH}_3)(\text{O})]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; $-\text{[P}(=\text{O})(\text{OH})(\text{CH}_2)]_m\text{-Q}$, where m is 0-3 and Q is a ribonucleoside connected via the ribose or the aromatic ring of the base; and an aryl group containing 0-3 substituents chosen independently from the group consisting of: Cl, Br, epoxy, acetoxy, $-\text{OG}$, $-\text{C}(=\text{O})\text{G}$, and $-\text{CO}_2\text{G}$, where G is independently selected from the group consisting of: $\text{C}_1\text{-C}_6$ straight alkyl, $\text{C}_2\text{-C}_6$ straight alkenyl, $\text{C}_1\text{-C}_6$ straight alkoyl, $\text{C}_3\text{-C}_6$ branched alkyl, $\text{C}_3\text{-C}_6$ branched alkenyl, $\text{C}_4\text{-C}_6$ branched alkoyl; and if E is aryl, E may be connected by an amide linkage;

e) if R_1 and at least one R_2 group are present, R_1 may be connected by a single or double bond to an R_2 group to form a cycle of 5 to 7 members;

f) if two R_2 groups are present, they may be connected by a single or a double bond to form a cycle of 4 to 7 members; and

g) if R_1 is present and Z_1 or Z_2 is selected from the group consisting of -
NHR₂, -CH₂R₂ and -NR₂OH, then R_1 may be connected by a single or double bond to the
carbon or nitrogen of either Z_1 or Z_2 to form a cycle of 4 to 7 members.

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